Paper No. 43

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte GREGORY R. REYES, DANIEL W. BRADLEY,
JR-SHIN TWU, MICHAEL A. PURDY, ALBERT W. TAM, and
KRZYSZTOF Z. KRAWCZYNSKI

Appeal No. 1997-0473
Application No. 07/870,985

ON BRIEF

Before WILLIAM F. SMITH, ROBINSON, and ADAMS, Administrative Patent Judges

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 15 - 18 and 20, which are all of the claims pending in this application.

Claim 15 is illustrative of the claims on appeal and is reproduced below:

15. A method of preventing or treating Hepatitis E Virus (HEV) infection in an individual, comprising

administering to the individual, by parenteral injection, a vaccine composition containing antibodies capable of neutralizing HEV infection, as evidenced by the ability of the composition to block HEV infection of primary human hepatocyte cells in culture, and where said composition contains an antibody which is immunoreactive with a peptide containing the C-terminal 48 amino acids of the capsid protein encoded by the second open reading frame of the HEV genome.

The references relied on by the examiner are listed below:

Webster's New World Dictionary of American English, Third College Edition, V. Neufeldt and D.B. Guralink eds., Simon & Schuster, Inc., New York, NY, p. 691 (1988)

Cohen, "Immunization," Basic & Clinical Immunology, Stites et al., eds., Lange Medical Publications, Los Altos, Ca., 4th edition, Chp. 39, pp. 703-706 (1982)

Bradley et al. (Bradley), "Enterically transmitted non-A, non-B hepatitis: Serial passage of disease in cynomolgus macaques and tamarins and recovery of disease-associated 27- to 34-nm viruslike particles," Proc. Natl. Acad. Sci., Vol. 84, pp. 6277-3281 (1987)

Grounds of Rejection

Claims 15 - 18 and 20 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on a non-enabling disclosure. As evidence the examiner relies on Webster's New World Dictionary of American English, Third College Ed. and Cohen

Claims 15 - 18 and 20 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Cohen and Bradley.

We reverse the rejection under 35 U.S.C. § 103 and vacate the rejection under 35 U.S.C. § 112, first paragraph, for the reasons set forth herein.

Background

Applicants describe their invention, as presently claimed, at pages 4-5 of the Specification as being directed to a method of preventing or treating a hepatitis E virus (HEV) infection in an individual by administering, thereto, an antibody vaccine composition capable of neutralizing HEV infection as evidenced by the ability of the composition to

block HEV infection of primary human hepatocyte cells in culture. Applicants state that the composition contains an antibody which is immunoreactive with a peptide containing the C-terminal 48 amino acids of the capsid protein encoded by the second open reading frame of the HEV genome.

Discussion

The rejection under 35 U.S.C. § 112, first paragraph

When an issue of enablement is raised under 35 U.S.C. § 112, first paragraph, the initial burden is on the Patent and Trademark Office to establish reasons why one skilled in the art would not believe the objective statements of utility and/or enablement in the specification. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

In setting forth the basis of the rejection under 35 U.S.C. § 112, first paragraph, it would reasonably appear that the examiner has premised his conclusion that the disclosure in support of the presently claimed invention is not enabling on two alternative propositions. First, the examiner urges that (Answer, page 3):

> the claimed method encompasses the prevention of HEV infection. Upon review of the specification of the subject application, no definition has been ascribed to the term "infection." In the absence of such guidance, the term "infection", . . . has been interpreted as "the fact or state of being infected, esp. by the presence in the body of bacteria, protozoans, viruses, or other parasites" (Webster's New World dictionary, Third College Edition). Given such an interpretation, the individual which is to receive the vaccine must not have HEV enter their body, else they would be infected with the virus. However, the antibody-comprising vaccine is incapable of such an effect as the vaccine acts by the binding of the antibodies to epitopes of HEV

> peptides/proteins/viral particles, thereby marking said viral peptides/proteins/viral particles for removal and ultimate destruction by phagocytic cells, e.g., macrophages.

Alternatively, the examiner urges that (Answer, page 4):

> the claimed method has been interpreted as though the antibody vaccine is administered only once. Given such an interpretation, the antibodies being administered have no capacity of regeneration/replenishment and will accordingly be eliminated from the individual, leaving the individual with no protective neutralizing capacity, much less a capacity to "prevent" an HEV invention. Even if the antibody were to be administered a plurality of times, the specification fails to provide sufficient guidance as to when, how often, and how much of the vaccine to administer in order to achieve "prevention" of HEV infection.

The examiner continues this analysis by noting that (Answer, page 5):

> At page 20, third paragraph, of the specification, the antibody is described as being comprised of "polyclonal antibodies from antisera, prepared for example, by immunization of a suitable animal, such as a rabbit or goat, with one of the HEV antigens above." . . . alternative sources include monoclonal antibodies produced by hybridoma using "lymphocytes from an immunized animal, preferably mouse or human" that are immortalized with a suitable fusion partner . . . A plurality of administrations of the vaccine would clearly potentiate the immune response of the individual against the foreign antibody which would only hasten its elimination from the system, leaving the individual with no means for preventing an HEV infection.
>
> This second proposition was raised in the non-final Office action of April 7, 1995

(Paper No. 28). However, the examiner failed to repeat this portion of the rejection in the final Office action of September 20, 1995 (Paper No. 31). We would observe, that since the examiner failed to refer to or repeat this portion of the rejection, the appellants may have considered this basis of rejection withdrawn. This is evidenced by the failure of the

appellants, in their Appeal Brief filed in response to the Final rejection, to offer any rebuttal to this particular basis of the rejection. While it is not readily apparent why the appellants chose not to file a Reply Brief as provided by 37 CFR § 1.193(b)(1) to respond to this new or reinstated basis of rejection, it remains that we have before us a record where the issues are not completely briefed by both parties.

In addition, we would note that the examiner initially acknowledges that the present disclosure is (Answer, paragraph bridging pages 3 and 4):

> enabling for a method of neutralizing hepatitis E virus (HEV) infection in an individual through passive immunization with a vaccine containing antibodies which are immunoreactive with an HEV peptide which contains the C-terminus 48 amino acid residues of the capsid protein by the second open reading frame of the HEV genome and where the amino acid residue sequence of said peptide contains an amino acid selected from the group consisting of SEQ. ID Nos. 13-20, ...

However, in the paragraph bridging pages 7-8 of the Answer, the examiner states that:

> there is no convincing evidence of record which reasonably enables the development and use of an antibody vaccine as a means of preventing and <u>treating</u> an HEV infection in an individual e.g., a human, nor is there convincing evidence of record which established the <u>in vitro</u> model as being an art accepted model of a human infected with HEV. (Emphasis added).

Since the specification and claims indicate that the vaccine used in the claimed method acts by neutralizing the HEV virus, on the record before us, it would appear that the examiner takes the position that the “treatment” of individuals with HEV infection is both enabled and non-enabled by the disclosure in support of the claimed invention.

Again, we have no response by appellants on this question. However, in view of the confusion about the status of what could reasonably be argued to be a new ground of rejection in the Examiner's Answer, the confusion as to just what the examiner regards as being enabled in the present case and the failure of both the examiner and appellants to completely brief the issues raised by this rejection, we conclude that this rejection and the issues raised thereby, is not presented in a form which would permit meaningful review. Therefore, as to the rejection of the appealed claims under 35 U.S.C. § 112, first paragraph, we vacate this rejection and remand the application to the examiner for reconsideration and/or clarification of the basis for questioning patentability on this basis. We would note that we do not authorize a supplemental examiner's answer to address the issues raised by this decision.

In view of our action with regard to this rejection it is not necessary for us to reach the issues raised by the examiner's arguments regarding whether the disclosure in support of the appealed claims are enabling for the "prevention" of HEV infection. However, we would note the we are less than enamored with the examiner's definition of infection and interpretation that "prevention of infection" would require that the virus in question be prevented from entering the body at any level. It is our opinion, that one skilled in this art, i.e., therapeutics or pharmacology, would, more likely than not, first turn to reference materials more associated with the field of pharmacology or therapeutics than a general

purpose dictionary in an effort to ascertain the meaning of the terms used in the present application. Further, as appellants point out at page 6 of the Brief:

> if the term were accorded the meaning advocated by the Examiner, the claim would be non-sensical to one of skill in the art (entry of a pathogen into a host cannot be prevented by antibodies within the host directed against the pathogen). On the other hand, if the term "preventing infection" is accorded the meaning advocated by the Appellants, the claim makes perfect sense to one of skill in the art.

In this regard we would emphasis that the disclosure submitted as part of the specification in an application for patent is directed to, and is to be understood by, one skilled in the art to which it relates. See Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997)("[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'") (Emphasis added).

The rejection under 35 U.S.C. § 103

Claims 15 - 18 and 20 stand rejected under 35 U.S.C. § 103 as being obvious over the combination of Cohen and Bradley.

In this rejection, the examiner relies on Cohen as describing "a general teaching of the benefits and concerns of using an antibody vaccine." (Answer, page 9). The examiner acknowledges that Cohen "does not teach the development of an antibody vaccine to hepatitis which is caused by HEV." (Id.). However, the examiner relies on Bradley as teaching (id.):

> the isolation of ET-NANBH, a.k.a., HEV or Hepatitis E Virus, as well as the development of experimental animals which are known to develop sera against the virus. . . [and notes] that antibodies which had been raised in both humans and in the primate models, in response to an ET-NANBH (HEV) infection, was purified.

The examiner concludes that (Answer, page 11):

> one of ordinary skill in the art at the time of the invention was made would have clearly been motivated to have utilized the sera produced by the monkeys taught by Bradley et alii, [sic] for a passive immunotherapy as disclosed by Cohen. Give [sic, Given] that Cohen teaches the development and use of passive therapy for a number of virally caused disease, including two types of hepatitis, the ordinary skilled artisan would have had a reasonable expectation of success.

It is sufficient for the purposes of this appeal to note that neither Bradley or Cohen describes, suggests or speculates on the possibility of developing a vaccine for HEV using antibodies capable of neutralizing HEV infection as required by the claims on appeal. As stated by appellants (Brief, paragraph bridging pages 8-9):

> Bradley, et al., do not teach any characterized sera, much less any specific epitopes of HEV, sequences or methods of identifying epitopes capable of generating neutralizing antibodies. And of course, Bradley, et al, do not teach that an antibody which is immunoreactive with a peptide containing the C-terminal 48 amino acids of the capsid protein encoded by the second open reading frame of the HEV genome is effective at neutralizing HEV or preventing HEV infection.

The examiner has not provided any evidence which would reasonably link the antibody vaccines described by Cohen with the sera generated antibodies of Bradley. In the absence of such evidence, the only suggestion to formulate a composition for the treatment and prevention of HEV infection in an individual, such as claimed in claim 15, is

provided by appellants' disclosure of the invention. However, use of this information as a basis for establishing a prima facie case of obviousness, within the meaning of 35 U.S.C. § 103, would constitute impermissible hindsight. There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the modifications required. That knowledge can not come from the applicant's invention itself. Diversitech Corp. v. Century Steps, Inc., 850 F.2d 675, 678-79, 7 USPQ2d 1315, 1318 (Fed. Cir. 1988); In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985). Thus, on this record, the examiner has not provided those facts or evidence which would reasonably support a conclusion that the claimed subject matter would have been prima facie obvious within the meaning of 35 U.S.C. § 103. Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir.1988). Therefore, the rejection of claims 15 - 18 and 20, under 35 U.S.C. § 103 as unpatentable over the combination of Cohen and Bradley is reversed.

SUMMARY

To summarize, the rejection of claims 15 - 18 and 20 under 35 U.S.C. § 112, first paragraph, is vacated. The rejection of claims 15 - 18 and 20 under 35 U.S.C. § 103 is reversed. The application is remanded to the examining group for consideration of the issues raised by this decision.

VACATED, REVERSED and REMANDED

WILLIAM F. SMITH	)
Administrative Patent Judge	)
	)
	)
	) BOARD OF PATENT
DOUGLAS W. ROBINSON)	
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
	)
DONALD E. ADAMS	)
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